

Amendments to the Specification

Please replace the paragraph beginning on page 9, line 37, with the following amended paragraph:

Fig. 3A ~~Fig. 3~~: Incremental succession of probes in a basic tiling strategy. The figure shows four probe sets, each having three probes. Note that each probe differs from its predecessor in the same set by the acquisition of a 5' nucleotide and the loss of a 3' nucleotide, as well as in the nucleotide occupying the interrogation position.

Please replace the paragraph beginning on page 10, line 7, with the following amended paragraph:

Fig. 4A ~~Fig. 4~~: Exemplary arrangement of lanes on a chip. The chip shows four probe sets, each having five probes and each having a total of five interrogation positions (I1-I5), one per probe.

Please replace the paragraph beginning on page 20, line 25, with the following amended paragraph:

In some reference sequences, every nucleotide is of interest. In other reference sequences, only certain portions in which variants (e.g., mutations or polymorphisms) are concentrated are of interest. In other reference sequences, only particular mutations or polymorphisms and immediately adjacent nucleotides are of interest. Usually, the first probe set has interrogation positions selected to correspond to at least a nucleotide (e.g., representing a point mutation) and one immediately adjacent nucleotide. Usually, the probes in the first set have interrogation positions corresponding to at least 3, 10, 50, 100, 1000, or 20,000 contiguous nucleotides. The probes usually have interrogation positions corresponding to at least 5, 10, 30, 50, 75, 90, 99 or sometimes 100% of the nucleotides in a reference sequence. Frequently, the probes in the first probe set completely span the reference sequence and overlap with one another relative to the reference sequence. For example, in one common arrangement each probe in the first probe set differs from another probe in that set by the omission of a 3' base complementary

to the reference sequence and the acquisition of a 5' base complementary to the reference sequence. See Fig. 3-Figs. 3A and 3B.

Please replace the paragraph beginning on page 21, line 35, with the following amended paragraph:

For conceptual simplicity, the probes in a set are usually arranged in order of the sequence in a lane across the chip. A lane contains a series of overlapping probes, which represent or tile across, the selected reference sequence (see Fig. 3-Figs. 3A and 3B). The components of the four sets of probes are usually laid down in four parallel lanes, collectively constituting a row in the horizontal direction and a series of 4-member columns in the vertical direction. Corresponding probes from the four probe sets (*i.e.*, complementary to the same subsequence of the reference sequence) occupy a column. Each probe in a lane usually differs from its predecessor in the lane by the omission of a base at one end and the inclusion of additional base at the other end as shown in Fig. 3-Figs. 3A and 3B. However, this orderly progression of probes can be interrupted by the inclusion of control probes or omission of probes in certain columns of the array. Such columns serve as controls to orient the chip, or gauge the background, which can include target sequence nonspecifically bound to the chip.

Please replace the paragraph beginning on page 22, line 15, with the following amended paragraph:

The probes sets are usually laid down in lanes such that all probes having an interrogation position occupied by an A form an A-lane, all probes having an interrogation position occupied by a C form a C-lane, all probes having an interrogation position occupied by a G form a G-lane, and all probes having an interrogation position occupied by a T (or U) form a T lane (or a U lane). Note that in this arrangement there is not a unique correspondence between probe sets and lanes. Thus, the probe from the first probe set is laid down in the A-lane, C-lane, A-lane, A-lane and T-lane for the five columns in Fig. 4 Fig. 4A. The interrogation position on a column of probes corresponds to the position in the target sequence whose identity is determined from analysis of hybridization to the probes in that column. Thus, I₁-I₅ respectively correspond

to N₁-N₅ in ~~Fig. 4~~ Fig. 4A. The interrogation position can be anywhere in a probe but is usually at or near the central position of the probe to maximize differential hybridization signals between a perfect match and a single-base mismatch. For example, for an 11 mer probe, the central position is the sixth nucleotide.

Please replace the paragraph beginning on page 33, line 7, with the following amended paragraph:

Some chips effectively contain the second, third and optionally, the fourth probes sets described in the basic tiling strategy (i.e., the mismatched probe sets) but omit some or all of the probes from the first probe set (i.e., perfectly matched probes). Therefore, such chips comprise at least two probe sets, which will arbitrarily be referred to as probe sets A and B (to avoid confusion with the nomenclature used to describe the four probe sets in the basic tiling strategy). Probe set A has a plurality of probes. Each probe comprises a segment exactly complementary to a subsequence of a reference sequence except in at least one interrogation position. The interrogation position corresponds to a nucleotide in the reference sequence juxtaposed with the interrogation position when the reference sequence and probe are maximally aligned. Probe set B has a corresponding probe for each probe in the first probe set. The corresponding probe in probe set B is identical to a sequence comprising the corresponding probe from the first probe set or a subsequence thereof that includes the at least one (and usually only one) interrogation position except that the at least one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the probe sets A and B. An additional probe set C, if present, also comprises a corresponding probe for each probe in the probe set A except in the at least one interrogation position, which differs in the corresponding probes from probe sets A, B and C. The arrangement of probe sets A, B and C is shown in Fig. 3B. Figure 3B is the same as ~~Fig. 3~~ Fig. 3A except that the first probe set has been omitted and the second, third and fourth probe sets in ~~Figure 3~~ Fig. 3A have been relabelled as probe sets A, B and C in Figure 3B.

Please replace the paragraph beginning on page 35, line 2, with the following amended paragraph:

When the chips comprise four probe sets, as discussed *supra*, and the probe sets are laid down in four lanes, an A lane, a C-lane, a G lane and a T or U lane, the probe having a segment exhibiting perfect complementarity to a reference sequence varies between the four lanes from one column to another. This does not present any significant difficulty in computer analysis of the data from the chip. However, visual inspection of the hybridization pattern of the chip is sometimes facilitated by provision of an extra lane of probes, in which each probe has a segment exhibiting perfect complementarity to the reference sequence. ~~See Fig. 4~~ Fig. 4A. This extra lane of probes is called the wildtype lane and contains only probes from the first probe set. Each wildtype lane probe has a segment that is identical to a segment from one of the probes in the other four lanes (which lane depending on the column position). The wildtype lane hybridizes to a target sequence at all nucleotide positions except those in which deviations from the reference sequence occurs. The hybridization pattern of the wildtype lane thereby provides a simple visual indication of mutations.